UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,275	03/28/2007	Ryozo Nagai	P30563	2170

7055 7590 07/12/2011

GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER	
PURDY, KYLE A	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
07/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

DETAILED ACTION

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/598,275
Filing Date: March 28, 2007
Appellant(s): NAGAI ET AL.

Bruce H. Bernstein, Reg. No. 29,027
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 4/22/2011 appealing from the Office action mailed 9/2/2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application: 24, 28, 29, 32, 33 and 37.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

WO 2001/80854	Shidoji et al.	04-2001
US 2005/0250671	Shidoji et al.	11-2005

Marx et al., Circ. Res., 2002, 90, 703-710

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 24, 28, 29, 32, 34 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marx et al. (Circ. Res., 2002, 90, 703-170) in view of Shidoji et al. (WO01/80854; published 04/23/2001) as evidenced by the English equivalent, US 2005/0250671.

Marx is directed to PPAR activators as anti-inflammatory mediators in human T lymphocytes. It's taught that activation of T lymphocytes and their ensuing elaboration of proinflammatory cytokines represents a critical step in atherogenesis and arteriosclerosis (see abstract). Marx also teaches that these proinflammatory cytokines are also integral to the development of transplantation-associated arteriosclerosis (Tx-AA) (see abstract). Marx shows that activation of PPAR results in marked reduction in cytokine mRNA expression and thus activation of PPAR limits the expression of proinflammatory cytokines yielding potential therapeutic benefits in pathological process like atherosclerosis and Tx-AA (see abstract). Marx is directed to PPAR activation in humans.

Marx fails to teach the administration of a polyprenylcarboxylic acid compound, specifically 3,7,11,15-tetramethyl-2,4,6,10,14 hexadecapentanoic acid (THA), as being a PPAR activator for treatment of arteriosclerosis.

Shidoji (the English equivalent) is directed to activators of peroxisome proliferative-activated receptors comprising the polyprenylcarboxylic compound, THA. It's taught that THA effectively activates PPAR (see [0009], Example 2 and [0028]). Shidoji teaches that THA is suitable for oral administration and may be combined with pharmaceutical carriers (additives) such as lactose and glucose (see [0019]). Shidoji teaches that THA is suitable for human consumption (see [0021]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Marx with Shidoji with a reasonable expectation for success in arriving at a method of treating arteriosclerosis by administering a polyprenylcarboxylic acid such as THA. Marx teaches that PPAR activation results in significant reduction in proinflammatory cytokines. Moreover, Tx-AA is characterized by smooth muscle cell proliferation, which is believed to be driven by cytokine and cytokine-induced growth factors. PPAR activation may oppose this response as the anti-inflammatory effects of PPAR activation on T lymphocytes contribute to decreased Tx-AA in patients. Although Marx fails to teach administering THA to elicit a PPAR response and treat arteriosclerosis, any ordinary person would have been capable of arriving at such. Shidoji teaches that THA is an excellent PPAR activator and can be administered orally with other pharmaceutical additives. Thus, an ordinary person would be motivated to select and administer THA on subjects with arteriosclerosis with a reasonable expectation in treating the said condition. With respect to the limitations that administration of the polyprenylcarboxylic acid treating arteriosclerosis such that activation of transcription factor KLF5 and vascular remodeling is inhibited, these are interpreted by the Examiner as inherent properties of administering polyprenylcarboxylic acid to treat arteriosclerosis. In other word, administering a polyprenylcarboxylic acid to a subject to treat arteriosclerosis would necessarily have the biological benefits espoused by Applicant, i.e. inhibition of KLF5 and vascular remodeling. Artisans of ordinary skill may not recognize the inherent characteristics or functions of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. With respect

to the limitation that the arteriosclerosis be due to vascular injury, wherein the vascular injury is the result of reconstructive surgery, this limitation is met by Marx because Marx teaches that arteriosclerosis may be associated with transplantation surgery, i.e. reconstructive surgery. Regardless, the means by which arteriosclerosis is formed is immaterial to the claim. Absent secondary considerations, it's the position of the Examiner that arteriosclerosis is arteriosclerosis, regardless of what caused it. In other words, arteriosclerosis caused by vascular surgery would be expected to be identical to arteriosclerosis not caused by vascular surgery, and therefore treatment with a polyprenylcarboxylic acid would reasonably be expected to treat each. Therefore, a method of administering a polyprenylcarboxylic acid for the treatment of arteriosclerosis is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

(10) Response to Argument

In response to the rejection of claims over 24, 28, 29, 32, 34 and 37 under 35 USC 103(a) over Marx et al. (Circ. Res., 2002, 90, 703-170) in view of Shidoji et al. (WO01/80854; published 04/23/2001) as evidenced by the English equivalent, US 2005/0250671, Appellant asserts the rejection is improper for the following reason(s):

A) Marx in view of Shidoji fails to teach or suggest a method wherein the activation of a transcription factor KLF5 is inhibited and/or wherein vascular remodeling is inhibited let alone a method of treatment for arteriosclerosis. There is no direction in either of the cited references to arrive at the instantly claimed methods;

B) Marx is directed to PPAR (peroxisome proliferator-activated receptors) activators on CD4+ T cells for reducing the effects of arteriosclerosis (transplant associated: Tx-AA) by reducing expression of proinflammatory cytokines whereas Shidoji is directed to PPAR activators comprising a polyprenyl compound, preferably (2E, 4E, 6E, 10E)-3,7,11,15-tetramethyl-2,4,6,10,14 hexadecapentanoic acid (THA herein), for the treatment of hyperlipidemia, non-insulin dependent diabetes mellitus or the like. Thus, not only would have having ordinary skill in the art not have combined the cited art references in the manner contended in the rejection, it would not have been obvious to treat arteriosclerosis with NIK-333 (aka THA) absent knowledge that such a compound inhibits KLF5 and/or inhibits vascular remodeling;

C) The Examiner contends that the reduction in the expression of proinflammatory cytokines from the activation of PPAR yields only "potential" therapeutic benefits in pathological processes such as arteriosclerosis and transplant associated arteriosclerosis. Thus, there is no reasonable expectation for success; and

D) Example 5 in Appellant's specification shows that THA provides more potent inhibitory action than ATRA (a comparative retinoid) against the proliferation of the tested 3T3-KLF5 cells in which KLF5 were stably expressed. Thus, the results illustrated in Example 5 establishes unexpected results and one of ordinary skill would not have expected the results found by Appellant.

In response to A, the Examiner respectfully disagrees and suggests that there is plenty of direction to arrive at the instantly claimed invention. Marx teaches that the activation of PPAR

reduces the expression of proinflammatory cytokines and that reduction in the expression of proinflammatory cytokines leads to decreased Tx-AA formation. Shidoji states that THA is a PPAR activator. The logical argument/conclusion based on the combination of Marx and Shidoji is as follows:

Administering a PPAR activator → treatment of arteriosclerosis;

THA → a PPAR activator; therefore,

Administering THA → treatment of arteriosclerosis.

Upon arriving at the obvious method of administering THA to treat arteriosclerosis, it follows then that any underlying biological mechanism and/or function [the inhibition of KLF5 and/or inhibition of vascular remodeling] related to the outcome of the method [treatment of arteriosclerosis via reducing inflammation] is an inherent property of such a method. That is, providing THA, a PPAR activator, to a mammal for the treatment of arteriosclerosis would necessarily inhibit KLF5 and/or inhibit vascular remodeling.

In response to B, one would not have to know the actual mechanism of action for THA in order to use it in a process of treating arteriosclerosis. As noted under the Examiners response to assertion A, the method of administering THA to treat arteriosclerosis is obvious and thus any underlying biological activity such as the inhibition of KLF5 and/or inhibition of vascular remodeling would necessarily be encompassed under such a method. With respect to Appellants argument that because Shidoji teaches treating disease with PPAR activators that are not taught by Marx, the combination of Marx and Shidoji is improper is not persuasive either. First, it's common knowledge that arteriosclerosis is associated with hyperlipidemia and so a population

with hyperlipidemia would overlap with a population having arteriosclerosis. Second, a PPAR activator is a PPAR activator. Providing any PPAR activator into the method of Marx would be obvious regardless of what other therapeutic processes (e.g. treatment of diabetes) that particular PPAR activator had been indicated as useful for. Thus, in view of at least these two reasons, any person of ordinary skill would envisage using THA in the method of Marx with a reasonable expectation for success in reducing inflammation associated with arteriosclerosis, thereby treating the arteriosclerosis.

In response to C, MPEP 2143.02 states that, "[A] rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in the respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art." Further, MPEP 2143.02 states that obviousness does not require absolute predictability, just some degree of predictability. The Examiners contends that the degree of predictability is moderately high as Marx teaches that PPAR activators may be implemented to reduce expression of inflammatory cytokines associated with Tx-AA thereby reducing inflammation associated with, and thus treating, Tx-AA. Appellants argument is not found persuasive.

In response to D, MPEP 2145 states that, "[T]he fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." Thus,

while the prior art does not recognize that administration of THA has any impact on KLF5, the art makes it quite clear that THA may be implemented in a method of treating arteriosclerosis. As arteriosclerosis is characterized by KLF5 expression, it would follow that administering THA to treat arteriosclerosis would necessarily inhibit KLF5 activation as the degree of arteriosclerosis is lessened. The recognition of latent properties [inhibition in KLF5 activation] in the prior art does not render nonobviousness an otherwise known invention. It follows that Appellant has not identified unexpected results rather Appellant has identified latent properties for an obvious invention.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/K. Purdy/
Examiner, Art Unit 1611

Conferees:

/SHARMILA G. LANDAU/

Supervisory Patent Examiner, Art Unit 1611

/David J Blanchard/

Supervisory Patent Examiner, Art Unit 1619